Message

From: Sue Chang [s.chang@mmm.com]
Sent: 5/11/2018 2:14:58 PM
To: Donohue, Joyce [Donohue.Joyce@epa.gov]
CC: Lau, Chris [Lau.Christopher@epa.gov]; Rogers, Emily [rogers.emily@epa.gov]
Subject: RE: published manuscript on PFHxS reproductive and developmental study in mice
Attachments: ATT00001.txt; Chang et al. 2017 Toxicol Sci 156 387-401.pdf

Hi Joyce,

The PFOS monkey study was published last year and it is attached here for you and Emily's reference. The conclusion remained the same in that the PFOS treatment-related effect that we observed in cynomolgus monkeys was a subtle lowering of cholesterol in our monkeys where they were followed for almost a year after dosing. The lower BMCL was 75 ug/mL.

Oh, I forgot to mention that we are also in the process of conducting a 90-day dietary study in mice with PFHxS. The study is on-going and we are in the early part of the second month test material administration.

We will, of course, be happy to discuss this (or our other studies that might be of interest to you and your team) in more details if you like. Thank you!

Regards,

Sue

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From: Donohue, Joyce [mailto:Donohue.Joyce@epa.gov]
Sent: Friday, May 11, 2018 8:53 AM
To: Sue Chang <s.chang@mmm.com>
Cc: Lau, Chris <Lau.Christopher@epa.gov>; Rogers, Emily <rogers.emily@epa.gov>
Subject: [EXTERNAL] RE: published manuscript on PFHxS reproductive and developmental study in mice

Dear Sue:

Thank you for sharing this information. I still receive bimonthly literature searches on the carboxylates and sulfonates so knew that the study had been published. We have a new staff member at EPA (Emily Rogers) who came to us from Oak Ridge and had helped out with the PFOS and PFOA Health Advisories while she was at Oak Ridge. She is writing up new

studies as we identify them so we are ready when we get inquiries. What is the status of the monkey study relative to publication?

I have copied Emily in my response to you so that you will have her contact information as well as mine.

I hope you all are well. I shall always be very thankful for the assistance you all provided when I was working on PFOS.

Joyce

From: Sue Chang [mailto:s.chang@mmm.com]
Sent: Friday, May 11, 2018 9:31 AM
To: Donohue, Joyce <Donohue.Joyce@epa.gov>
Cc: Lau, Chris <Lau.Christopher@epa.gov>
Subject: FYI: published manuscript on PFHxS reproductive and developmental study in mice

Hi Joyce,

Long time no talk, hope this note finds you well. During our last visit a couple of years back while we discussed our new PFOS monkey study with you and your team, we had informed you that we were planning on some sort of subchronic study with perfluorohexanesulfonate (PFHxS). Well, fast forward to 2018, we had completed a modified OECD 422 study in CD-1 mice and the study has now been accepted and published. The final manuscript is included here for your reference.

If you recall, we had done and published an OECD 422 study for PFHxS in rats in 2009 (Butenhoff et al 2009 Reproduct Toxicol 27 331-341). In that study, there were no test material-related effects on either reproduction or development in rats. Albeit the serum elimination half-life in (non-pregnant) female rats is much faster than male rats (~ 2 days and 30 days, respectively), the highest maternal serum PFHxS concentration achieved in our rat study was still around 60 ug/mL at LD 21, which was quite appreciable. Given that we do know the serum elimination profiles between (non-pregnant) female mice and male mice are much similar (~ 30 days), we undertook a new reproductive study with PFHxS in CD-1 mice to address the uncertainties associated with the differences in TK (that was observed in rats).

In our current study with CD-1 mice, we were able to achieve the following serum concentrations:

~180 ug/mL on study day 14 in female mice prior to mating;
~111 ug/mL at GD 18 for dams (~ 137 ug/mL for fetus); and
~137 ug/mL at LD 22 for dams (~60 ug/mL for pups)

In addition, pups were directly dosed with PFHxS (at the same respective maternal doses) from PND 22 and on for 2 weeks (and through sexual maturation stage) and at PND 36, the serum concentration in pups were approximately 180 ug/mL with no gender difference seem in serum TK in these developing pups.

Based on our current study findings, there were no PFHxS treatment-related effects on reproduction, neonatal mortality, pup survival, pup body weights, body weight-gain, or attainment of sexual maturation. These findings are consistent with our previous findings in rats, but, at much higher body burden in both dams and pups. Also, when compared to PFOS at similar (molar) concentration ranges from both rats and mice repro studies, we did not see the neonatal mortalities that were reported for PFOS. Overall, we believe that all these studies (rats or mice) support the fact that the toxicity potency of PFHxS in rodents is lower than PFOS.

Please let me know if there are any questions. Thank you!

Sue

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